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# Guidelines for postoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations — Part II

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## HIGHLIGHTS

- We provide evidence supporting postoperative management of patients undergoing gynecologic/oncology surgery.
- This guideline will help integrate knowledge into practice, align perioperative care, and encourage future investigations.

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## ABSTRACT



## 1. Introduction

The "Guidelines for Pre- and Intra-operative Care in Gynecologic/Oncology Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations — Part I," [1] examined the evidence surrounding care elements including preoperative medical optimization, bowel preparation, carbohydrate loading, thromboembolism prophylaxis, skin preparation, standard anesthetic protocol and intraoperative fluid management. The goal of this article is to critically review existing evidence and make recommendations for elements of postoperative care. This effort forms the basis of the ERAS® Guideline for postoperative care in gynecologic/oncology surgery.

## 2. Methods

### 2.1. Literature search

The authors convened in July 2014 to discuss topics for inclusion — the topic list was based on the ERAS® Colonic Surgery [2] and Rectal/

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Pelvic [3] Guidelines which were used as templates. After the topics were agreed upon they were then allocated amongst the group according to expertise. The literature search (1966–2014) used Embase and PubMed to search medical subject headings including "gynecology", "gynecologic oncology" and all postoperative ERAS® items (see Table 1). Reference lists of all eligible articles were crosschecked for other relevant studies.

### 2.2. Study selection

Titles and abstracts were screened by individual reviewers to identify potentially relevant articles. Discrepancies in judgment were resolved by the lead (GN) and senior authors (OL, SD). Meta-analyses, systematic reviews, randomized controlled studies, non-randomized controlled studies, reviews, and case series were considered for each individual topic.

### 2.3. Quality assessment and data analyses

The quality of evidence and recommendations were evaluated according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system (see Tables 2a and 2b) [4] whereby recommendations are given as follows: Strong recommendations indicate that the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident. Recommendations are based on quality of evidence: high, moderate, low and very low but also on the balance between desirable and undesirable effects; and on values and preferences. As such, consistent with other ERAS® Guideline Working groups [2,5], in some cases strong recommendations may be reached from low-quality data and vice versa. Of note, this would be considered a modified GRADE evaluation since we did not consider resource utilization when making our recommendations [6].

**Table 2a**
GRADE system for rating quality of evidence.

| Evidence level | Definition |
|---|---|
| High quality | Further research unlikely to change confidence in estimate of effect |
| Moderate quality | Further research likely to have important impact on confidence in estimate of effect and may change the estimate |
| Low quality | Further research very likely to have important impact on confidence in estimate of effect and likely to change the estimate |
| Very low quality | Any estimate of effect is very uncertain |

Reference [4].

## 3. Results

The evidence base, recommendations, evidence level, and recommendation grade are provided for each individual ERAS® item below.

**Table 1**
Guidelines for postoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations.

| Item | Recommendation | Evidence level | Recommendation grade |
|---|---|---|---|
| Prophylaxis against thromboembolism | Patients should wear well-fitting compression stockings and have intermittent pneumatic compression | High | Strong |
| | Extended prophylaxis (28 days) should be given to patients after laparotomy for abdominal or pelvic malignancies | High | Strong |
| Postoperative fluid therapy | Intravenous fluids should be terminated within 24 h after surgery; balanced crystalloid solutions are preferred to 0.9% normal saline | Moderate | Strong |
| Perioperative nutritional care | A regular diet within the first 24 h after gynecologic/oncology surgery is recommended | High | Strong |
| Prevention of postoperative ileus | The use of postoperative laxatives should be considered | Low | Weak |
| | The use of chewing gum should be considered | Moderate | Weak |
| Postoperative glucose control | ERAS elements that reduce metabolic stress should be employed to reduce insulin resistance and the development of hyperglycemia | High | Strong |
| | Perioperative maintenance of blood glucose levels (<180–200 mg/dL) results in improved perioperative outcomes; glucose levels above this range should be treated with insulin infusions and regular blood glucose monitoring to avoid the risk of hypoglycemia | High | Strong |
| Postoperative analgesia | A multimodal approach to analgesia should be adopted including use of NSAIDS/acetaminophen, gabapentin and dexamethasone (unless contraindications exist) | Multimodal: high<br>NSAIDS/aceta: high<br>Gabapentin: moderate<br>Dexamethasone: low | Strong |
| | Vaginal hysterectomy | | |
| | Paracervical nerve block or intrathecal morphine can be used to reduce pain and opioid consumption | Low | Weak |
| | Open general gynecologic surgery | | |
| | Spinal anesthesia with intrathecal morphine is recommended | Moderate | Strong |
| | Alternatively, thoracic epidural analgesia (TEA) with low concentration local anesthetic solutions with the addition of opiates for 24-48 h can be considered | High | Strong |
| | Truncal nerve blocks (TAP or ilioinguinal) can be recommended where patients have undergone general anesthesia without neuraxial blockade | Moderate | Strong |
| | Continuous wound infiltration (CWI) of local anesthetic can be considered | Moderate | Strong |
| | Major oncologic surgery | | |
| | TEA may be considered but patients frequently require additional IV opioids in addition to TEA to achieve adequate analgesia | Low | Weak |
| | Laparoscopic gynecologic/oncology surgery | | |
| | Lack of evidence makes it difficult to recommend one analgesic intervention over another, however a multimodal approach should be employed | Low | Weak |
| Peritoneal drainage | Peritoneal drainage is not recommended routinely in gynecologic/oncology surgery including for patients undergoing lymphadenectomy or bowel surgery | Moderate | Strong |
| Urinary drainage | Urinary catheters should be used for postoperative bladder drainage for a short period preferably <24 h postop | Low | Strong |
| Early mobilization | Patients should be encouraged to mobilize within 24 h of surgery | Low | Strong |

**Table 2b**
GRADE system for rating strength of recommendations.

| Recommendation strength | Definition |
|---|---|
| Strong | When desirable effects of intervention clearly outweigh the undesirable effects, or clearly do not |
| Weak | When trade-offs are less certain — either because of low quality evidence or because evidence suggests desirable and undesirable effects are closely balanced |

Reference [4].

## 4. Postoperative thromboembolism prophylaxis

### *4.1. Immediate postoperative prophylaxis*

Pneumatic compression stockings reduce the rate of VTE (venous thromboembolism) when compared to observation [7]. The risk reduction is equivalent when compared to heparin [8] and improved when combined with heparin [9] in gynecologic oncology patients. Graduated compression stockings decrease the rate of DVT in hospitalized patients, especially when combined with another method [10].

### *4.2. Extended postoperative prophylaxis*

A large prospective cohort trial showed an increased rate of VTE within 30 days of surgery in cancer patients [11], and extended prophylaxis (28 days) is now considered a common practice within major gynecologic oncology surgery [12]. A Cochrane review of 4 randomized controlled trials examining extended prophylaxis has shown a decrease in VTE (14.3% vs. 6.1%; $p < 0.0005$) and a decrease in symptomatic VTE (1.7% vs. 0.2%; $p = 0.02$) [13]. The role of extended prophylaxis in minimally invasive surgery is likely not necessary without other high-risk features (elevated BMI, previous VTE, coagulopathy, decreased mobility) [14].

#### *4.2.1. Summary and recommendations*

Patients should wear well-fitting compression stockings and have intermittent pneumatic compression. Extended prophylaxis (28 days) should be given to patients after laparotomy for abdominal or pelvic malignancies.

#### *4.2.2. Evidence level*

High.

#### *4.2.3. Recommendation grade*

Strong.

## 5. Postoperative fluid therapy

Oral intake of fluid and food should be started the day of surgery whenever possible. With the commencement of oral diet and oral analgesia as soon as tolerated after surgery the need for postoperative intravenous fluids beyond 12–24 h is rarely needed in an uncomplicated recovery. Patients can drink immediately after surgery. Flavored high energy protein drinks prescribed three times a day are safe and can bridge the postoperative period of building back up to a normal diet to ensure some protein and calorie intake early in the recovery process. They are usually 200–250 ml in volume with around 150 kJ/100 ml of carbohydrate and 3–6 g/100 mL of protein with the addition of vitamins, mineral and trace elements. If intravenous fluids must be maintained then a total hourly volume of no more than 1.2 mL/kg (including drugs, approximately 90 mL/h for a 75 kg female) should be given [15]. Balanced crystalloid solutions are preferred to 0.9% normal saline due to the cumulative risk of hyper-chloremic acidosis. The use of starch solutions during the perioperative period should be limited by dose and duration to avoid the adverse effects seen in studies on intensive care patients such as bleeding and renal dysfunction [16]. Oliguria as low as 20cm$^3$/h is a normal response to surgery, and the need for further intravenous fluid boluses should be assessed within clinical context. A small proportion of patients undergoing major surgery will develop SIRS (Systemic Inflammatory Response Syndrome) causing marked vasodilation and hypotension without sepsis. These patients will require vasopressor therapy such as a noradrenaline infusion during surgery and postoperatively until resolution.

### *5.1. Summary and recommendations*

Intravenous fluids should be terminated within 24 h after surgery. Balanced crystalloid solutions are preferred to 0.9% normal saline.

### *5.2. Evidence level*

Moderate.

### *5.3. Recommendation grade*

Strong.

## 6. Perioperative nutritional care

A number of randomized trials on the subject of early feeding (defined as having oral intake of fluids or food within the first 24 h after surgery) have been performed in gynecologic oncology [17–20]. Effects include accelerated return of bowel activity, reduced length of stay, with no evidence of higher complication rates related to wound healing, anastomotic leaks, or pulmonary complications. A randomized study in patients with ovarian cancer showed a significantly lower rate of complications for patients receiving early feeding. However, complication rates were not different between groups when the analysis was limited to a smaller cohort of patients undergoing intestinal resections [18,19]. It is important to note that early feeding is associated with a higher rate of nausea, but not vomiting, abdominal distension, or nasogastric tube use. Patient satisfaction with control of vomiting in one series was over 90% with early feeding despite a higher incidence of nausea in the enhanced recovery group [21].

### *6.1. Summary and recommendation*

A regular diet within the first 24 h after gynecologic/oncology surgery is recommended.

### *6.2. Evidence level*

High.

### *6.3. Recommendation grade*

Strong.

## 7. Prevention of postoperative ileus

Laxatives are commonly used within enhanced recovery protocols to hasten the return of bowel function, but no high quality data is available in gynecologic oncology. In one prospective, but nonrandomized trial of 20 patients undergoing open radical hysterectomy, milk of magnesia and biscolic suppositories were well tolerated and associated with a reduction in hospital stay compared with historical controls [22]. In 68 patients undergoing hepatic resection via laparotomy, patients randomized to magnesium hydroxide experienced a median one-day reduction in time to passage of stool [23]. Although data are limited and effects appear modest, continued use of laxatives is reasonable given the low cost and side effect profile.

In patients undergoing hysterectomy and colonic resection, randomized trials have shown improved recovery when a peripheral mu antagonist was administered [24]. Its use in patients undergoing planned enteric resections is reasonable, but we cannot provide a recommendation for its use at the present time as cost-effectiveness and efficacy data in patients with gynecologic malignancies continues to be collected. Perioperative use of chewing gum had a positive effect on the incidence of postoperative ileus (36% vs. 15%) and length of stay (1 day reduction) in a randomized trial of patients undergoing staging for gynecologic malignancies [25]. A meta-analysis of randomized trials investigating prokinetics such as erythromycin, the cholecystokinin-like drugs, cisapride, dopamine-antagonists, propranolol, vasopressin, and intravenous lidocaine [26] or neostigmine [27] failed to demonstrate benefit.

### 7.1. Summary and recommendations

The use of postoperative laxatives and chewing gum should be considered.

### 7.2. Evidence level

Laxatives: Low.
Chewing gum: Moderate.

### 7.3. Recommendation grade

Weak.

## 8. Postoperative control of glucose

Perioperative hyperglycemia, classically defined as blood glucose levels greater than 180 to 200 mg/dL is associated with poor clinical outcomes including increased perioperative mortality, hospital length of stay, ICU length of stay and postoperative infection [28,29]. Most clinicians would agree that prevention of perioperative hyperglycemia is a desirable intervention, the optimal blood glucose range remains controversial due to the potential adverse events related to iatrogenic hypoglycaemia [30]. Clinical trials in adult surgical patients illustrate this paradigm of outcomes with intensive insulin therapy (IIT) defined as 140 to 200 mg/dL by the American College of Physicians. The Leuven surgical trial randomly assigned patients to IIT or conventional glucose management with a decrease in mean blood glucose levels and ICU mortality in the IIT group [31]. However, hypoglycemia was more frequent in the IIT group. These findings were supported by meta-analytical data from 5 randomized trials, which compared IIT to less stringent glycemic control and demonstrated significantly lower mortality [32]. In contrast, the Normoglycemic in Intensive Care Evaluation Survival Glucose Algorithm Regulation (NICE-SUGAR) trial demonstrated a higher rate of severe hypoglycemia and higher 90-day mortality in those patients who received IIT compared to conventional glucose management [33]. Hypoglycemia is the most common adverse effect of IIT and can lead to unwanted morbidity such as seizures, brain damage, and cardiac arrhythmias. As a result, more liberal blood glucose targets of 180 to 200 mg/dL are typically recommended in effort to prevent significant hyperglycemia whilst avoiding iatrogenic hypoglycemia [34–36].

The surgical stress response triggers a cascade of sympathetic nervous system and endocrine responses that include activation of the HPA axis and increased cortisol secretion, which leads to a net increase in peripheral insulin resistance [37]. Traditional perioperative interventions such as mechanical bowel preparation, pre-operative fasting, and slow resumption of normal diet all contribute to the relative insulin resistant state noted perioperatively and have been shown to correlate with perioperative complications and increased length of hospital stay [38]. Several elements of enhanced recovery protocols abrogate postoperative insulin resistance and thereby result in lower perioperative glucose levels without resulting hypoglycemia. Examples of key elements include avoidance of oral mechanical preoperative bowel preparation and avoidance of preoperative fasting until 2 h prior to surgery, pre-operative carbohydrate loading along with stimulation of gut function by early resumption of postoperative oral intake and optimal fluid balance [1].

### 8.1. Summary and recommendation

ERAS elements that reduce metabolic stress should be employed to reduce insulin resistance and the development of hyperglycemia. Perioperative maintenance of blood glucose levels (<180–200 mg/dL) results in improved perioperative outcomes. Glucose levels above this range should be treated with insulin infusions and regular blood glucose monitoring to avoid the risk of hypoglycemia.

### 8.2. Evidence level

Use of stress reducing elements: High.
Treating hyperglycemia above 180–200 mg/dL: High.

### 8.3. Recommendation grade

Strong.

## 9. Postoperative analgesia

Pain following gynecological abdominal surgery can be severe [39]. Uncontrolled acute post-operative pain is associated with dissatisfaction [40], post-operative complications, and is a strong risk factor for development of chronic pain [41]. Morphine is commonly used to control post-operative pain but is associated with nausea, sedation [42], fatigue [43] and poorer quality of recovery [44] and may prolong time to mobilization. Opioid analgesics also contribute to the development of ileus. Therefore an enhanced recovery pathway for gynecological surgery must employ a strategy to effectively control post-operative pain and allow attainment of other ERAS targets such as early mobilization and return to oral diet whilst reducing the need for opiates. Many RCTs in the last 20 years in open surgery have focused on epidural analgesia, which can offer excellent analgesia, reduction in the surgical stress response, and earlier return of gut function. However the role of epidural analgesia is now a matter of debate. With the increasing uptake of laparoscopic and robotic assisted surgery the magnitude and duration of visceral and wound pain have been markedly reduced such that good post-operative pain control is achievable by many different analgesic techniques, often used in combination to tackle both the visceral and wound elements. The literature base is developing rapidly and may well impact on future recommendations.

### 9.1. Multimodal analgesia

The concept of achieving analgesia through the additive or synergistic effects of different types of analgesics is not new [45]. Non-steroidal anti-inflammatory drugs (NSAIDs) have been extensively investigated, both as part of a multi-modal analgesic regime as well as for gynecologic surgery, and are effective at reducing pain and opioid consumption and improving patient satisfaction [46,47], and a combination of NSAID and acetaminophen is more effective than either drug alone [48]. Both should be administered regularly unless contraindication exists. Gabapentin has recently become popular for treatment of post-operative pain. A recent systematic review found that pre-emptive administration of gabapentin for abdominal hysterectomy was effective in reducing post-operative pain, opioid consumption and side effects [49] and has been used in one gynecologic enhanced recovery program [21]. However, studies have not yet identified the optimal dose, or timing of administration. Dexamethasone appears to have analgesic

effects [50,51], as well as preventing post-operative nausea and vomiting, so may be useful as part of an ERP for gynecologic surgery. However its analgesic effects are yet to be fully investigated and it may cause transient post-operative hyperglycemia. Chronic administration of steroids are known to impair wound healing, although this has not been demonstrated following administration of a course <10 days duration [52]. Intravenous lidocaine is gaining popularity as an analgesic adjunct in abdominal surgery. A Cochrane analysis concluded that there was low quality evidence of an early reduction in pain, and opioid consumption and time to bowel recovery were reduced, though the effect on these outcomes was small [26].

*9.1.1. Summary and recommendations*

A multimodal analgesia strategy should be employed with the aim of reducing post-operative opioid requirement. Post-operatively, opioids should be given orally to patients who can tolerate diet. For patients unable to tolerate diet following surgery, then an opioid IV PCA can be used until resumption of GI function, but the oral route should be used as soon as possible.

Acetaminophen and NSAIDs in combination should be administered regularly to all patients unless contraindication exists.

Dexamethasone may be administered to prevent PONV and reduce pain, but should be used with caution in diabetic patients.

Gabapentin may reduce pain and side effects and may be considered, although the optimal dose is not known.

*9.1.2. Level of evidence*

Use of multimodal analgesia: High.
Combination of acetaminophen and NSAIDs: High.
Gabapentin: Moderate.
Dexamethasone as an analgesic: Low.

*9.1.3. Recommendation grade*

Strong.

*9.2. Analgesia for vaginal hysterectomy*

Few rigorous studies have been performed investigating analgesia in patients undergoing vaginal hysterectomy. In one study, intra-operative paracervical nerve block appeared to reduce post-operative pain and morphine consumption, and although the analgesic benefit appears to be limited to the first few hours after surgery, patients mobilized more quickly [53]. However a Cochrane review concluded that paracervical nerve block was ineffective for cervical dilatation [54]. One study investigated high-volume local anesthetic infiltration of the surrounding tissues and found that although the analgesic benefit was limited to the first four hours post-operatively, patients used less opioid analgesics and mobilized earlier [55]. In another study, spinal anesthesia with intrathecal morphine and clonidine also reduced early post-operative pain and morphine consumption, though the effect was modest [56]. Both spinal morphine and paracervical nerve block have been used to facilitate early discharge in enhanced recovery vaginal hysterectomy pathways [57,58].

*9.2.1. Summary and recommendations*

Local anesthetic infiltration may be effective at reducing early post-operative pain and opioid consumption, and facilitating early mobilization. Either paracervical nerve block or intrathecal morphine may reduce pain and opioid consumption after vaginal hysterectomy. However, the effect is small.

*9.2.2. Evidence level*

Low.

*9.2.3. Recommendation grade*

Weak.

*9.3. Analgesia for open general gynecologic surgery*

The optimal analgesic regimen for open gynecologic surgery is currently a subject of debate. Thoracic epidural analgesia (TEA) has gained widespread acceptance in providing post-operative analgesia for major abdominal surgery [2], and has been shown to be superior to intravenous PCA [59]. TEA is effective in attenuating the surgical stress response and reducing pain and opioid consumption for up to 72 h [59,60] following abdominal incisions, and also has an impact on complications following abdominal surgery, reducing the time to bowel recovery by up to 36 h and may reduce cardiac and respiratory complications in high risk patients. TEA has been shown to effectively reduce pain following abdominal hysterectomy [61] and gynecologic cancer surgery [62], and reduces time to return of gut function. However the role of TEA in enhanced recovery surgery is now less clear: whilst analgesia and recovery seem to be better with TEA than IV PCA, epidural failure rates may be as high as 30% [63], and many of these patients will require supplemental opiates. Even if patients are normovolemic the sympathetic block that results from TEA may result in hypotension that may require treatment with vasopressors [64]. Patients who undergo abdominal hysterectomy in ERAS protocols can target a length of hospital stay of 1–2 days, in which case TEA may hinder achievement of other ERAS goals such as mobilization [65] and removal of urinary catheter, and TEA has been shown to increase hospital stay and complication rates in gynaecologic cancer surgery [66].

Where TEA is to be used local anesthetic should be of low concentration, and should be combined with an opioid such as fentanyl. Post-operative hypotension may require treatment with vasopressors. Some consideration must be made to the impact on early ERAS goals and how they will be achieved, and expert post-operative input may be required to ensure reliable analgesia. Although epidurals sited in the lumbar spine have an evidence base for analgesic benefit in gynecologic surgery, thoracic epidurals are preferred: epidurals should be sited at the level appropriate for innervation of the surgical area, and thoracic epidurals are likely to cause less hypotension [67] and motor block [68] than those in the lumbar segments.

An alternative to TEA is spinal anesthesia with low-dose intrathecal morphine (ITM). As a single injection, this has benefits over TEA in allowing early mobilization and removal of urinary catheter as well as facilitating early discharge from hospital [69]. When compared to a general anesthetic without neuraxial block, spinal anesthesia with ITM significantly reduces pain and morphine consumption both for hysterectomy [39,44,70] and this analgesic benefit may persist for up to 48 h post-operatively [39,44]. The added benefit of reduced morphine consumption is the reduced risk of post-operative ileus. Additionally ITM appears to reduce peri-operative stress hormone release [71], improve post-operative recovery [44,72] and reduce post-operative drowsiness and fatigue, though at the expense of increased pruritus [73]. Most studies do not indicate an increase in vomiting with low-dose ITM when compared with IV PCA [39,74]. Dose-finding studies appear to show a ceiling of effect at 200 mcg [74] and doses of ITM within this range do not appear to increase the risk of respiratory depression [75]. Spinal anesthesia without long-acting opioids does not improve post-operative pain when compared to general anesthesia [76].

Experience dictates that to improve patient acceptability of spinal anesthesia with ITM, general anesthesia may need to be offered in addition, in which case the dose of intrathecal local anesthetic should be reduced to avoid intra-operative hypotension and intraoperative narcotics should be minimized to reduce side effects.

Where patients have undergone general anesthesia without neuraxial blockade, truncal nerve blocks may serve to reduce pain and reduce post-operative morphine requirement. Transversus abdominis plane (TAP) blocks involve the injection of a large volume of local anesthetic in between the muscle layers of the trunk, and may now be performed under ultrasound guidance to ensure accurate delivery of local anesthetic. This technique has been shown to be efficacious for

abdominal incisions [77], including abdominal hysterectomy [78], and a meta-analysis concluded that TAP blocks reduce pain and morphine requirement up to 24 h after open gynecologic surgery [79]. In patients undergoing Cesarean section, TAP blocks appear to be less effective than intrathecal morphine at controlling post-operative pain, although side effects were fewer than ITM [80] and TAP blocks do not appear to add any analgesic benefit when used in combination with ITM [81]. Bilateral ilioinguinal nerve blocks also appear to reduce post-operative morphine requirement, however may not reduce morphine-related side effects [82].

Wound infiltration with local anesthetic is safe and easy to perform, though any effect on post-operative pain and opioid consumption is modest and short-lived [83]. Prolongation of this analgesic effect may be achieved through insertion of sub-cutaneous wound catheters [84]. A meta-analysis concluded that continuous wound infiltration (CWI) reduced pain and opioid consumption and improved recovery after major abdominal surgery [85], and may provide analgesia equivalent to TEA for abdominal surgery [86]. Another study found that, when compared to TEA for open colorectal surgery, CWI reduced opioid usage, vomiting and time to bowel recovery, and improved patient satisfaction [87]. However for gynecologic surgery the data is less clear, and although CWI has been shown to improve analgesia, reduce opioid requirements and reduce time to return of gut function [88] a number of studies have either only demonstrated benefit in the first few hours after surgery [84], or failed to demonstrate benefit at all [89–91]. There is lack of agreement concerning ideal catheter placement [92, 93], though in most studies the infusion catheter was placed below the abdominal fascia. The impact of continuous wound infiltration on wound healing has not been fully studied, though existing data has not shown an increase in wound complication rates. More research with this technique is required in this patient group before any conclusions may be drawn.

Intraperitoneal local anesthetic (IPLA) has been utilized to reduce post-operative pain, and one trial demonstrated reduced opioid consumption and improved surgical recovery score when used alongside TEA following colorectal surgery [94]. A systematic review of other trials concluded that IPLA reduces post-operative pain but not opioid consumption, and recovery parameters were unchanged [95]. IPLA has also been tested for open hysterectomy and has been found to reduce post-operative pain [96] and morphine consumption [97], however the benefit was limited to the first few hours after surgery, and analgesia from IPLA does not seem to be dose-responsive [98].

#### 9.3.1. Summary and recommendations

For open surgery a multimodal, opiate sparing analgesic strategy should be utilized. TEA or spinal anesthesia with intrathecal morphine may improve recovery parameters and are recommended. However TEA may increase time to mobilization and removal of urinary catheter, and may potentially impact on hospital stay.

Where patients have undergone general anesthesia without neuraxial blockade, a truncal block, such as TAP blocks, may reduce pain and opioid consumption for up to 24 h and should be employed. Continuous wound infiltration or intraperitoneal instillation of local anesthetic may improve recovery for colorectal surgery and may be considered as an alternative to TAP blocks or TEA, however the evidence of benefit in gynecologic surgery is lacking.

Post-operatively, multimodal analgesia should be used. Systemic opioids may be given either orally or by intravenous PCA. The IV PCA should be discontinued when normal gut function resumes.

#### 9.3.2. Evidence level

Intrathecal morphine: Moderate.
Thoracic epidural analgesia: High.
TAP blocks: Moderate.
CWI: Moderate.

#### 9.3.3. Recommendation grade

Strong.

### 9.4. Analgesia for major oncologic surgery

In patients undergoing cytoreductive surgery, the large surgical area and complex patient pain history means that post-operative pain is often severe. TEA is widely used, and was associated with superior pain control at rest and on movement for the first 3 post-operative days in one observational study [99], and a randomized controlled study [100] found improved pain control on coughing for the first 3 post-operative days. However other investigators found no benefit in pain, bowel recovery or length of stay in patients with peri-operative TEA, and an increase in vasopressor requirement [101]. In patients undergoing heated intraperitoneal chemotherapy (HIPEC), the use of TEA is controversial. TEA may reduce opioid consumption and reduce time to extubation [102] although an IV PCA is often required in addition to TEA to achieve adequate analgesia [103]. HIPEC may be associated with a post-operative coagulopathy that may complicate removal of the epidural catheter, however in one study removal of epidural catheter was delayed in only 0.5% of cases [104]. Some centers use intravenous PCA in preference to TEA, citing adequate analgesia with fewer hemodynamic effects [105]. TAP blocks were examined in one retrospective study and appeared to reduced opioid consumption on post-operative day 1 only [106].

#### 9.4.1. Summary and recommendations

TEA is effective in reducing post-operative pain after gynecologic laparotomy. However TEA may not improve other post-operative outcomes and patients may require additional IV opioids in addition to TEA to achieve adequate analgesia. TEA may compound hypotension that requires vasopressor support. Intravenous PCA appears to be a suitable alternative.

#### 9.4.2. Evidence level

Low.

#### 9.4.3. Recommendation grade

Weak.

### 9.5. Analgesia for laparoscopic gynecologic/oncology surgery

A meta-analysis examining TAP blocks for laparoscopic surgery across a range of abdominal procedures [107] found only pain at rest, and not dynamic pain, was reduced. For laparoscopic hysterectomy, one trial showed that TAP blocks improved post-operative quality of recovery (QoR40) score [108] however 3 further trials did not show benefit [109–111]. Intra-peritoneally administered local anesthetic has been used successfully for minor gynecologic laparoscopic procedures but this technique does not seem to be effective for major gynecologic laparoscopic surgery, either by single instillation or continuous infusion [112–116]. Additionally, a Cochrane analysis of intraperitoneal local anesthetic for laparoscopic cholecystectomy found low quality evidence of benefit, though the effect was likely to be clinically insignificant [117]. ITM showed a small benefit in robotic surgery [118]. TEA has been investigated for laparoscopic colorectal surgery and appeared to prolong hospital stay without improving patient outcomes [69].

#### 9.5.1. Summary and recommendations

For laparoscopic gynecologic/oncology surgery, neither TAP blocks nor intraperitoneal instillation of local anesthetic are recommended on the current level of evidence. For laparoscopic abdominal surgery, TEA may prolong hospital stay without improving outcomes. Multimodal analgesia should be employed, and post-operative opioids may be given either orally or by IV PCA depending on magnitude of surgery and predicted post-operative gut function.

*9.5.2. Level of evidence*

Low.

*9.5.3. Recommendation grade*

Weak.

## 10. Peritoneal drainage

Peritoneal drainage has traditionally been used to prevent accumulation of fluid in the bed of dissection, to evacuate blood, serous collections, or infection, and in colorectal surgery it has been thought to prevent anastomotic leakage. However, peritoneal drainage has not been shown to prevent anastomotic leaks or improve overall outcome, and is not recommended routinely after either colonic or rectal surgery [119–121]. There is little research regarding drains after colonic or rectal anastomosis in gynecologic oncology surgery [122]. It is difficult to extrapolate the results from the colorectal literature directly to all gynecological surgery. For patients with metastatic ovarian cancer, the scope of surgery is larger, encompassing other organ resections, most of the peritoneal surfaces, and the risk factor profile for postoperative morbidity is elevated with poor nutritional status, ascites, peritoneal carcinomatosis, extended operative times, and cytotoxic therapy. Regardless, the rate of anastomotic leakage in ovarian cancer surgery in the literature ranges from 1 to 7%, in the range found in colorectal surgery [122–124]. In summary, we did not find evidence that drainage gives better outcomes after gynecological surgery. Furthermore, a Cochrane systematic review including 4 studies with 571 participants [125] concluded that drains did not prevent lymphocysts, but were rather associated with a higher risk of cyst formation after pelvic lymphadenectomy. Fewer studies have investigated para-aortic lymphadenectomy, but no evidence exists to recommend drainage [126]. Urological surgical techniques are frequently employed during major gynecologic oncology cases. Historically drains have been placed at the site of bladder resection/reconstruction, ureteral reimplantation, and urinary diversion (ileal conduit, continent reservoir) with the aim of identifying early urine leaks. Nevertheless, there are no specific studies that have evaluated the use of drains in such surgeries in our patient population. Looking to the urological literature, it should be noted that the ERAS Radical Cystectomy guideline found no evidence to support or refute the use of drains in this setting and as such further research is required in this area [5].

*10.1.1. Summary and recommendation*

Peritoneal drainage is not recommended routinely in gynecologic/oncology surgery including for patients undergoing lymphadenectomy or bowel surgery.

*10.1.2. Evidence level*

Moderate.

*10.1.3. Recommendation grade*

Strong.

## 11. Urinary drainage

The primary indications for postoperative bladder drainage are to monitor urine output and prevent urinary retention. However, there is considerable variation in the method and duration of bladder drainage following surgery for gynecological cancers. In addition, there is a high incidence of bladder related morbidity to the lower genital tract following such surgery, which may include effects on urinary voiding and bladder capacity [127].

A review of policies for removal of short-term urinary catheters identified only a small number of studies including patients undergoing gynecologic surgery [128]. When comparing the timing of removal of the catheter, time to first voiding was longer, but larger volumes of urine were passed following midnight removal compared to early morning. In one study, midnight removal of catheters was also associated with significantly shorter length of stay [129]. A recent single center study following uncomplicated total abdominal hysterectomy compared removal of urethral catheters immediately after surgery, 6 h, or 24 h postoperatively. The intermediate group had fewer re-catheterizations compared to the immediate removal group, and lower rates of urinary tract infection than the prolonged users [130]. These findings are supported by a recent review [131]. In the same review, a greater number of patients required re-catheterization following a urethral compared to a suprapubic catheter. Two small studies focusing on patients undergoing radical hysterectomy for cervical cancer showed the suprapubic route to be associated with fewer bladder infections [132,133]. In one of these studies intermittent self- catheterization was associated with a higher infection rate but patients found the technique to be catheterization [133].

*11.1.1. Summary and recommendation*

Urinary catheters should be used for postoperative bladder drainage for a short period preferably <24 h postoperatively.

*11.1.2. Evidence level*

Low.

*11.1.3. Recommendation grade*

Strong.

## 12. Early mobilization

There are multiple hypothesized benefits to early mobilization, including a reduction in pulmonary complications, decreased insulin resistance, less muscle atrophy, and reduced length of hospital stay [134,135]. Early mobilization has been shown to be an integral part of systematic efforts to reduce venous thromboembolic complications in the surgical patient [136]. Foley catheters, poor pain control, and IV poles, have been identified by gynecologic surgical patients as barriers to ambulation [137]. Therefore, compliance with other aspects of enhanced recovery protocols may improve early mobilization by limiting these barriers [138]. A care plan listing daily mobilization goals and patient engagement with an activity diary may be helpful [135,139].

*12.1.1. Summary and recommendation*

Patients should be encouraged to mobilize within 24 h of surgery.

*12.1.2. Evidence level*

Low.

*12.1.3. Recommendation grade*

Strong.

## 13. Discussion

This guideline outlines the recommendations of the ERAS® Group for the postoperative management of patients undergoing gynecologic/oncology surgery, and is based on the best available evidence. As was the case in Part I [1], in some instances good quality data was not available. This was particularly true for the evidence surrounding urinary drainage, early mobilization and postoperative analgesia in which the

optimal analgesic regimen for vaginal surgery/MIS and open gynecologic surgery is currently a subject of debate. In some instances recommendations were made based on findings from other surgical disciplines in which major abdominal surgery is routinely utilized.

We are hopeful that these gynecologic/oncology ERAS® guidelines will help integrate existing knowledge into practice, align perioperative care, and encourage future investigations to address existing knowledge gaps. Measuring compliance has proven to be a key factor required for success and sustainability of ERAS® protocols [140]. A process is currently underway whereby the gynecologic/oncology guidelines are being translated into their corresponding audit system (ERAS Interactive Audit System, EIAS) which will help to ensure compliance [141] and allow surgeons/clinicians to improve the care delivered to our patient population.

#### Conflict of interest statement

Dr. Acheson reports personal fees from Baxter UK Ltd., outside the submitted work. In addition, Dr. Acheson has a commercial (future royalties on a medical device in development) relationship with Mediplus Ltd. He has also held the following appointments: Joint National Clinical Advisor (Gynaecology) to the Enhanced Recovery Partnership Programme, Department of Health (2010–2011), and continued under NHS Improvement (2011–2013); Member of Steering Board, Enhanced Recovery ERAS (UK) (2011–2013).

Dr. Scott received honoraria for lecturing and travel expenses from Baxter Healthcare, Merck, and Deltex. He is an Executive Committee member of the ERAS Society.

Dr. Ljungqvist has an appointment with Nutricia Advisory Board, has received speakers honoraria from Nutricia, MSD, BBraun and Fresenius-Kabi. He is the current Chairman of the ERAS Society (www.erassociety.org). He founded, serves on the Board and owns stock in Encare AB that runs the ERAS Society Interactive Audit System (EIAS).

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